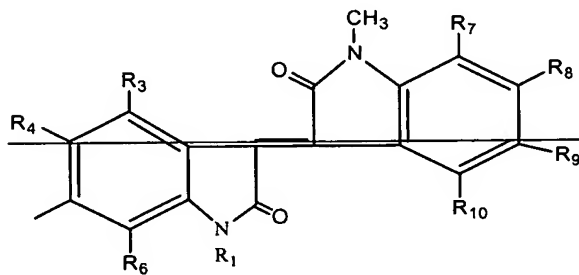
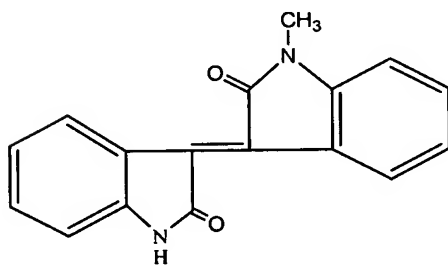


## AMENDMENTS TO THE SPECIFICATION

Please replace Formula (IV) on page 16 with the following formula:

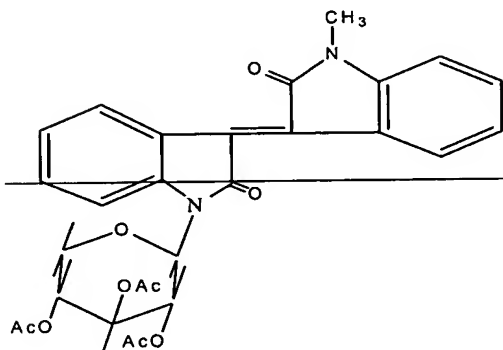


**FORMULA (IV)**

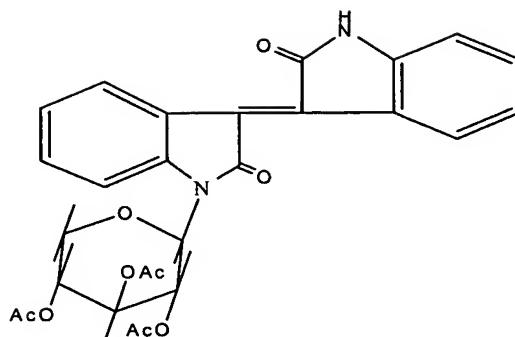


**FORMULA (IV)**

Please replace Formula (VI) on page 16 with the following formula:



**FORMULA (VI)**



**FORMULA (VI)**

Please replace the last paragraph on page 25, and continuing onto page 26 with the following amended paragraph:

-- Psoriasis: Cytokines are intercellular messengers that have an important role in the development and maintenance of cutaneous inflammation. A number of cytokines have been reported to play crucial roles in the pathogenesis of inflammatory skin disorders. IL-1, TNF- $\alpha$ , and IFN- $\gamma$  induce expression of ICAM-1 and major histocompatibility complex (MHC) class II (48, 49). IL-1, TNF- $\alpha$ , and granulocyte-macrophage colony-stimulation factor are able to induce activation, maturation, and migration of dendritic cells, and IL-1 activates mast cells (50). IL-6 and TGF- $\alpha$  enhance keratinocyte proliferation. IL-1, TNF- $\alpha$ , TGF- $\alpha$ , and VEGF induce angiogenesis and attract inflammatory cells (51-53). The primacy of cytokines in eliciting cutaneous immune responses makes them a highly attractive target for new biological response modifiers (18). Therefore, as multi-cytokines regulators, the small molecules claimed in this invention, Meisoindigo and derivatives of isoindigo, indigo and indirubin will be effective against psoriasis. ~~As shown in Example 6, we demonstrated in a rodent model that Meisoindigo was truly effective in a dose-dependent manner against psoriasis and the effect was better than the positive control MTX.~~ --

Please delete all of Example 6, beginning on page 40 with the heading "Example 6: Meisoindigo Enhances Epidermal Cell Differentiation and Inhibits Hyperplasia and Hyperkeratosis in Rodents," and ending on page 43, with the first full paragraph starting with "The mouse-tail model used in this Example".

Please replace the heading of the example beginning on page 43, with the following amended heading:

-- Example [[7]] 6: Meisoindigo Suppresses Induced Acute Ulcerative Colitis in Balb/c MiceMaterials and Methods --

Please replace the first full paragraph on page 44 with the following amended paragraph:

-- Induction of Acute Ulcerative Colitis DSS-induced colitis in Balb/c Mice: Colitis was induced by DSS in drinking water (MW 36,000 – 50,000, ICN biochemicals) as described previously (~~112~~)(106). Briefly, the mice were randomly divided into 3 groups composed of 10 mice each. In the negative control group (Group 1), mice were given fresh tap water ad libitum and MF pellets, freshly changed twice a week, for 7 days. In the positive control group (DSS group, or Group 2), 5% DSS in tap water was given for 7 days to induce colitis, and the mice were fed with MF pellets. In the DSS-Meisoindigo group (test group or Group 3), mice were given 5% DSS drinking water and given Meisoindigo orally once a day at a dose of 50 mg/kg for 7 consecutive days. Fecal indications of colitis were recorded daily, including body weight and nature of feces (loose and/or bleeding or occult blood). Mice were then sacrificed. Colon tissues were taken, fixed in 10% formalin/PBS, and embedded in paraffin. To minimize physical artifacts, the removed colon was put onto a thick qualitative filter paper without stretching. The colon was then exposed inside out by cutting it longitudinally. The slides were stained with H&E and blindly examined histochemically by 3 technician/pathologists. --

Please replace the heading of the example beginning on page 45, with the following amended heading:

-- Example [[8]] 7: Meisoindigo Completely Halted Idiopathic Inflammatory Bowel Disease In a Patient --

Please replace the first full paragraph on page 45 with the following amended paragraph:

-- Patient: A ~~43-years~~ 43-year old woman was diagnosed as having over a four-year period, a case of active chronic proctocolitis with erosion and features suggestive of idiopathic inflammatory bowel disease. The first diagnosis was performed at North Shore University Hospital Manhasset, Long Island, New York in 1999 by colonoscopy. Major symptoms included diarrhea, loose stool and bleeding while her overall condition of health was considered excellent. Clinical-activity index (Table 5) ~~(113)~~ (107) was determined to be between 7 and 8. Her physician prescribed hydrocortisone foam, which she administered for 10 days according to doctor's instructions. However, no therapeutic effect was obtained from this agent. In February 2000, she returned to her home in China and on several occasions, visited Chinese physicians and tried various Chinese herbal medicines suggested, but no therapeutic effect was observed. In early 2002, she went to a well-known and respected Chinese Medical Hospital in Beijing where Flexible Sigmoidoscopy was performed. Again, she was diagnosed as having active inflammatory bowel disease. --

Please replace all of the paragraphs on page 58 with the following amended paragraphs:

-- 102. Kong, M., Barnes, E. A., Ollendorff, V., and Donoghue, D. J. Cyclin F regulates the nuclear localization of cyclin B1 through a cyclin-cyclin interaction. *Embo J*, *19*: 1378-1388, 2000.

103. McGovern, S. L. and Shoichet, B. K. Kinase inhibitors: not just for kinases anymore. *J Med Chem*, *46*: 1478-1483, 2003.

104. Group, C. Phase III clinical trials of Meisoindigo on the treatment of chronic myeloid leukemia. *J. Chinese Hematology*, *18*: 69-72, 1997.

105. Tang, X., Fenton, M. J., and Amar, S. Identification and functional characterization of a novel binding site on TNF-alpha promoter. *Proc Natl Acad Sci U S A*, *100*: 4096-4101, 2003.

~~106. Bosman, B., Matthiesen, T., Hess, V., and Friderichs, E. A quantitative method for measuring antipruritic activity of drugs by the mouse tail test. *Skin Pharmacol*, *5*: 41-48, 1992.~~

~~107. Jarrett, A. The physiology and pathophysiology of the skin. *Lancet*, *2*: 445, 1973.~~

- ~~108.—Sebok, B., Szabados, T., Kerenyi, M., Schneider, I., and Mahrle, G. Effect of fumaric acid, its dimethylester, and topical antipsoriatic drugs on epidermal differentiation in the mouse tail model. Skin Pharmacol, 9: 99-103, 1996.~~
- ~~109.—Sebok, B., Bonnekoh, B., Kerenyi, M., and Gollnick, H. Tazarotene induces epidermal cell differentiation in the mouse tail test used as an animal model for psoriasis. Skin Pharmacol Appl Skin Physiol, 13: 285-291, 2000.~~
- ~~110.—Feldman, S. R., Garton, R., Averett, W., Balkrishnan, R., and Vallee, J. Strategy to manage the treatment of severe psoriasis: considerations of efficacy, safety and cost. Expert Opin Pharmacother, 4: 1525-1533, 2003.~~
- ~~111.—Liu, X. M., Wang, L. G., Li, H. Y., and Ji, X. J. Induction of differentiation and down-regulation of c-myb gene expression in ML-1 human myeloblastic leukemia cells by the clinically effective anti-leukemia agent meisoindigo. Biochem Pharmacol, 51: 1545-1551, 1996.~~
- [[112.]] 106. Okayasu, I., Hatakeyama, S., Yamada, M., Ohkusa, T., Inagaki, Y., and Nakaya, R. A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology, 98: 694-702, 1990.
- [[113.]] 107. Lichtiger, S., Present, D. H., Kornbluth, A., Gelernt, I., Bauer, J., Galler, G., Michelassi, F., and Hanauer, S. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med, 330: 1841-1845, 1994. --